Comparison of myocardial contrast enhancement via cardiac magnetic resonance imaging in healthy cats and cats with hypertrophic cardiomyopathy

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Objective—To quantify myocardial contrast enhancement (MCE) of the left ventricle (LV) by use of cardiac magnetic resonance imaging (CMRI) in healthy cats and cats with hypertrophic cardiomyopathy (HCM) and to compare MCE between the 2 groups.

Animals—10 healthy cats and 26 Maine Coon cats with moderate to severe HCM but without clinical evidence of congestive heart failure.

Procedure—Anesthetized cats underwent gradient echo CMRI examination. Short-axis images of the LV were acquired before and 7 minutes after IV administration of gadolinium dimeglumine. Regions of interest were manually traced in the quadrants of 5 mid-LV slices acquired at end systole, and the MCE percentage was calculated from summed weight-averaged data from all slices. Doppler tissue imaging echocardiography was performed to measure the early diastolic myocardial velocity (Em) as an index of diastolic function. Three-way repeated-measures ANOVA was used to determine differences in MCE between cats with HCM and healthy cats. Simple linear regression was used to assess whether MCE was correlated with LV mass, LV mass index (LVMI), or Em. A Student t test was used to compare the SDs of the postcontrast myocardial signal intensity between the 2 groups.

Results—There was no difference in MCE between cats with HCM and healthy cats. There was no correlation of MCE with LV mass, LVMI, or Em. There was no difference in heterogeneity of signal intensities of LV myocardium between the 2 groups.


Contrast-enhanced cardiac magnetic resonance imaging (CMRI) is a noninvasive imaging technique used to diagnose myocardial fibrosis or necrosis in humans with hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy, Becker’s muscular dystrophy, and myocardial infarction. For the procedure, a low–molecular-weight paramagnetic contrast agent is administered IV. The contrast material is distributed in the extracellular (interstitial) space in the myocardium, reabsorbed by the capillary bed, and excreted by the kidneys. In areas of abnormal myocardium, the contrast agent accumulates in the extracellular space and has a slow washout period (ie, 6 to 20 minutes). In patients with myocardial fibrosis, the extracellular space is expanded because of myocardial loss and production of collagen. Expansion of the extracellular space results in pooling of the agent (gadolinium) and a slow washout. On T1-weighted images, delayed enhancement (DE) of the myocardium appears hyperintense (bright) as a result of accumulation of contrast medium. Delayed-enhancement MRI was first used to assess myocardial infarction in which regions of nonviable myocardium appear hyperintense and areas of normal and hibernating myocardium have normal intensity. Most (80%) asymptomatic to mildly symptomatic patients have patchy areas of DE in hypertrophied areas of the left ventricular (LV) myocardium. Results of 1 histologic study confirmed that regions of DE correspond to regions of myocardial fibrosis. Assessment of myocardial fibrosis may yield important clinical information, such as risk of development of congestive heart failure or sudden death in patients with HCM. Delayed-enhancement MRI has also been performed in hamsters with cardiomyopathy in which areas of myocardial DE were histologically confirmed to be regions of replacement fibrosis, interstitial fibrosis, and inflammation.

The Maine Coon cats used in the present study had familial HCM, which has previously been histopathologically characterized by interstitial and replacement fibrosis as well as LV myofiber disarray. Myocardial fibrosis and hypertrophy may lead to diastolic dysfunction and development of congestive heart failure. Doppler tissue imaging (DTI) echocardiography is a useful, noninvasive method for assessing diastolic function in humans and other animals. Decreased early diastolic myocardial velocity (Em) develops with substantial diastolic dysfunction. Reduced Em develops in cardiac diseases that are associated with myocardial fibrosis and is negatively correlated (r = −0.7) with the percentage of interstitial fibrosis in myocardial tissue from humans with coronary artery disease and LV dysfunction.
Noninvasive methods for assessing the extent of myocardial fibrosis in veterinary patients have not been published. The use of contrast enhancement CMRI in cats with HCM has not been reported. If affected cats had evidence of DE of the myocardium on MRI, serial evaluation might be useful to monitor changes in myocardial fibrosis after pharmacologic treatment.

The hypotheses of the study reported here were that cats with moderate to severe HCM would have measurable evidence of DE and would have greater myocardial contrast enhancement (MCE) on CMRI than healthy cats. The purposes of the study were to develop a quantitative method for assessing MCE, perform CMRI in healthy cats and cats with HCM, and determine whether there was a correlation between MCE and LV mass or diastolic function.

Materials and Methods

Ten healthy cats without evidence of cardiac disease as determined by results of echocardiographic imaging and 24 MCA and Maine Coon-cross cats from a colony with hereditary mild to severe HCM (mild, 6- to 7-mm wall thickness; moderate, 7 to 8 mm; severe, > 8 mm; reference limit, < 5.5 mm) were used in this study. Cats with HCM had concentric hypertrophy of the LV (ie, LV wall or interventricular septal thickness ≥ 6 mm) but had neither clinical signs of congestive heart failure nor evidence of other diseases that could cause concentric hypertrophy of the LV. The mean age of healthy cats was 5.4 years (range, 3.33 to 8.25 years), and the mean age of cats with HCM was 4.9 years (range, 1.08 to 11.8 years). Three cats (11%) with HCM had evidence of mild to moderate left atrial enlargement on imaging, with a left atrial diameter-to-aortic diameter ratio of 1.51 to 1.53 (normal, < 1.5).

Cats were anesthetized with propofol administered as a continuous rate infusion and intubated; anesthesia was maintained with positive-pressure ventilation. T1-weighted CMRI images were acquired with a 1.5T magnet and parallel 3-inch-diameter surface coils during multiple phases of the cardiac cycle. A gradient-echo sequence with the following settings was used: field of view, 12 cm²; echo time, 5.2 milliseconds; repetition time, 12.1 milliseconds; flip angle, 30°; number of excitations, 1; matrix, 256 × 128 pixels; and spatial resolution, 0.5 × 0.9 mm. Cardiac gating was triggered from the R wave of the electrocardiogram. By use of initial 3-plane localizer images, a 4-chamber long-axis view was chosen. Short-axis images of the LV were acquired during hyperventilation-induced apnea every 3 mm from the mitral valve annulus to the LV apex. After images were acquired, gadolinium dimeglumine was administered as an IV bolus at a dose of 0.1 mmol/kg and postcontrast images were acquired 7 minutes later.

Images were obtained before and after contrast enhancement and were analyzed at the end of systole. The LV was divided into 4 quadrants: cranial free wall, interventricular septum, caudal free wall, and lateral free wall. Slices 5 through 8 were analyzed because those slices represented the middle section of the LV with the greatest myocardial area. Mean signal intensities (SIs) were calculated in each quadrant of all 4 LV slices from operator-defined regions of interest (ROIs), which were drawn to avoid the hypertensive blood pool or partial-volume-averaged regions of intermediate myocardial SIs (Figure 1). An additional ROI of air within the lower right field of view was also drawn in each image and used to standardize myocardial SIs. The relative intensity (RI) of the myocardium was defined as $SI_{myocardium}/SI_{air}$ and that value was used to correct for variation in magnetic field intensity between slices and studies. All images were evaluated for evidence of increased regional SIs of the myocardium (ie, DE), which would indicate myocardial fibrosis. Myocardial contrast enhancement is the percentage change of myocardial RI between pre- and postcontrast images and was calculated from values for myocardial RI before and after contrast injection by use of the following equation: $MCE = \frac{(RI_{before \, contrast} - RI_{after \, contrast})}{RI_{before \, contrast}} \times 100$. An LV mass was quantified by use of the Simpson rule, as described. The LV mass index (LVMI) was calculated as gram of LV mass per kg.

On a separate day, cats were sedated with 0.1 mg of acepromazine/kg and 0.1 mg of hydromorphone/kg administered SC and DTI echocardiography was performed. With a 12-MHz probe, DTI of the lateral portion of the mitral annulus was performed from the left apical 4-chamber view, with the pulsed-wave Doppler gate placed perpendicular to myocardial movement. Settings included the following: Nyquist limit, 10 to 15 cm/s; sweep speed, 100 cm/s; gate width, 0.11 cm; and filter, 50 Hz. Five consecutive measurements of peak diastolic velocity were recorded, and a mean Em was calculated. An ECG was obtained to measure heart rate.

Three-way repeated-measures ANOVA was performed, with grouping factor, region, and slice as the within factors, to assess whether MCE in healthy cats was different from that in cats with HCM. The mean of the 4 highest MCE values/cat (maxMCE) was calculated, and simple linear regression was used to assess whether maxMCE was correlated with LV mass, LVMI, or diastolic DTI velocity. Likewise, the mean of the 4 lowest MCE values/cat (minMCE) was calculated, and simple linear regression was used to assess whether minMCE was correlated with LV mass, LVMI, and diastolic DTI velocity. To assess whether there was a difference in variation of SIs between the groups (ie, assess myocardial heterogeneity), the mean SD of the postcontrast SIs in cats with HCM was compared with that in healthy cats by use of a paired Student t test. Values of $P <$ 0.05 were considered significant.

Results

One cat with HCM, but no healthy cats, had discrete DE of LV myocardium (Figure 2). In that cat, discrete DE...

Figure 1—T1-weighted cardiac magnetic resonance image (CMRI) of the heart of a Maine Coon cat with hypertrophic cardiomyopathy (HCM). Image was obtained before contrast agent (gadolinium dimeglumine) was administered, at the level of the sixth short-axis slice of the left ventricle (LV). Images of the LV were analyzed for myocardial contrast enhancement (MCE). The LV was divided into quadrants (1 through 4), and regions of interest were drawn within the myocardium to obtain mean myocardial signal intensity (SI) and SD of the SI within the region of interest. The SI of air (quadrant 5) was also recorded. Myocardial contrast enhancement was calculated with the values for myocardial relative intensity before and after administration of gadolinium. R = Right, Cr = Cranial, L = Left, Cd = Caudal.
was observed in the cranial portion of the LV free wall, in
the area of the most severe hypertrophy. There was no
difference in MCE between healthy cats and cats with
moderate to severe HCM ($P = 0.8$). Mean MCE in healthy
and affected cats was 31% and 30%, respectively. There
was no difference in MCE between regions or between
LV slices ($P = 0.9$ and 0.7, respectively).

There was a weak correlation between LVMI and
minMCE in healthy cats and cats with HCM ($R = 0.44; P = 0.01$) and no correlation between LV mass or LVMI
and maxMCE (Figure 3). Cats with HCM had decreased Em, compared with healthy cats (cats with
HCM: mean Em, 8.9 ± 2.5 cm/s; healthy cats: mean
Em, 12 ± 1.7 cm/s; $P = 0.02$). There was no correlation
between Em and minMCE or maxMCE in healthy cats
and cats with HCM ($R = 0.1$ and 0.2, respectively).

There was no difference in SDs of the postcontrast
myocardial SIs between healthy cats and cats with
HCM ($P = 0.3$), indicating that there was no difference
in heterogeneity of SIs of the LV myocardium between
the groups.

**Discussion**

Unlike humans with HCM, Maine Coon cats with
familial HCM rarely have evidence of DE of the
myocardium on gradient-echo CMRI and do not have
increased heterogeneity of myocardial SIs. There was a
weak correlation of minMCE with LVMI, a finding that
may be associated with decreased myocardial perfusion
in cats with high values for LVMI. In the study report-
ed here, only 1 of 26 cats had discrete DE of the
myocardium; that cat was 8 years old and had severe
HCM, with DE detected in the region of greatest
myocardial hypertrophy (cranial portion of LV free
wall). That region likely represented a large area of
fibrosis, but this was not confirmed histologically.

These findings were in contrast to reported frequency
of DE in humans with asymptomatic or mildly symp-
tomatic HCM, in which 80% of patients have evidence
of DE on CMRI. Delayed enhancement in those
patients is observed only in the hypertrophied regions
of the LV, has a patchy to multifocal distribution, and
predominantly involves the middle third of the LV
wall. Regions of DE are histologically characterized
by replacement and interstitial fibrosis. Given the
spatial resolution of contrast CMRI, replacement fibro-
sis is most likely the type of fibrosis detected. Detection of diffuse interstitial fibrosis by DE is limited
because the technique is sensitive to regional differ-
ences in gadolinium accumulation. Delayed enhance-
ment is observed in < 50% of human patients with
dilated cardiomyopathy and diffuse interstitial fibro-
sis. In the study reported here, if the voxel resolution
of contrast MRI with a 12-cm$^2$ field of view and a
matrix of 256 × 128 pixels were approximately 0.5 ×
0.9 × 3 mm, it is likely that only macroscopic scarring
would have been visible by DE. Maine Coon cats that
die of severe familial HCM develop both interstitial
and replacement fibrosis of the LV. In our study, the cats
with HCM did not have clinical signs of congestive

![Figure 2—T1-weighted CMRI of the heart of a Maine Coon cat
with HCM before (A) and after (B) administration of a contrast
agent. Notice the asymmetric pattern of hypertrophy and a
large, discrete region of delayed enhancement (arrow) in the
region of the cranial LV free wall. RV = Right ventricle. See
Figure 1 for remainder of key.]

![Figure 3—Simple linear regression of minimal myocardial con-
trast enhancement versus LV mass index (LVMI) in healthy cats
(n = 10) and cats with HCM (26). The mean of the 4 lowest
myocardial contrast enhancement values/cat was calculated.
$R = 0.44; P = 0.01$. $Y = 2.8 - 2.2X$.](http://example.com/figure3.jpg)
heart failure and had less severe disease than those examined previously by means of histologic analysis. Cats may have had interstitial fibrosis, a change that would be less evident in contrast enhancement CMRI. Our findings were limited by the lack of histologic examination of myocardial tissues to confirm and assess the extent of myocardial fibrosis. Histologic evaluation of the study cats was not possible because they were to be enrolled in another study.

Assessment of myocardial fibrosis may yield important clinical information, such as the risk for developing congestive heart failure or sudden cardiac death in patients with HCM. Regional heterogeneity of diastolic function has been diagnosed with CMRI in humans and develops in regions of extensive myocardial fibrosis. In humans with HCM, the extent of DE is correlated with the extent of diastolic dysfunction. Serial measurement of myocardial fibrosis during the course of treatment could be useful to detect a reduction in the severity of myocardial fibrosis and, consequently, decreased risk of adverse cardiac events. Unfortunately, noninvasive techniques for assessment of myocardial fibrosis are limited. In a randomized alldactone evaluation study, serum markers of collagen synthesis and degradation were measured to indirectly quantify the extent of myocardial fibrosis in humans with congestive heart failure before and during treatment with an aldosterone antagonist. Patients with high baseline serum concentrations of collagen markers were at greatest risk of sudden cardiac death, and patients with large reductions in serum concentrations of collagen markers were more likely to have better survival rates and fewer cardiovascular complications.

In conclusion, contrast enhancement CMRI was not useful for quantification of myocardial fibrosis in Maine Coon cats with HCM. The technique continues to be a valuable tool for quantifying LV mass in cats. 

References